§Appl. No. 10/009,500

Amdt. dated August 23, 2004

Reply to Office Action of, April 21, 2004

REMARKS

Restriction

SEQ ID NOS. 1, 3, 5, and 7 all code for proteins with manillase (hyaluronidase) properties. See, specification, Page 6, lines 5-7. The attached sequence alignment (Exhibit 1) shows that the amino acid sequences are highly related, sharing at least about 93% identity (about 454/488) between all four isoforms, with high sequence identity between the individual pairs. In a teleconference with Examiner Patterson, it was agreed that Applicant would submit such evidence for his consideration. In view of this submission, it is requested that the restriction between the various forms be withdrawn.

Sequence

The specification has been amended to conform to the sequence rules by adding sequence identifiers to the unidentified sequences. These sequences were already listed in the sequence listing filed February 4, 2003.

Rejection under §101

Claim 20 has been amended to conform with U.S. practice. Support for the amendment can be found throughout the specification, including Page 2, line 27-Page 4, line 9.

Rejections under §112, second paragraph

Claim 16 has been amended to a pharmaceutical composition. Support for the amendment can be found throughout the specification, including Page 6, lines 25-26.

Claims 7, 18, and 19 have been amended to clarify them; these amendments do not change the claim scope, but merely clarify what the skilled worker would have understood from the claim's original wording.

12

MERCK-2332

§Appl. No. 10/009,500

Amdt. dated August 23, 2004

Reply to Office Action of, April 21, 2004

Rejections under §102

It is believed that amendment to claim 18 renders this rejection moot.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

Richard M. Lebovitz, Reg. No. 37,067

Attorney for Applicant(s)

MILLEN, WHITE, ZELANO & BRANIGAN, P.C. Arlington Courthouse Plaza 1, Suite 1400 2200 Clarendon Boulevard

Arlington, Virginia 22201

Telephone: (703) 243-6333 Facsimile: (703) 243-6410

Attorney Docket No.: MERCK-2332

Date: August 23, 2004

13

MERCK-2332

EXHIBIT

1

CLUSTAL W (1.82) multiple sequence alignment

SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	KEIAVTIDDKNVIASVSESFRGVAFDASLFSPKGLWSFVDITSPKLFKLLEGLSPGYFRV KEIAVTIDDKNVIASASGSFLGVAFDASLFSPKGLWSFVDITSPKLFKLLEGLSPGYFRV	60 60 60
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	GGTF ANWER FOLDENING WAS ADATE ETAIL TRANSPORTED TO THE TOTAL	120 120 120 120
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	SKMRLLFDLNAEVRTGYEIGKKMTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNEPDHTS SKMRLLFDLNAEVRTGYEIGKKTTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNEPDHTS SKMRLLFDLNAEVRTGYEIGKKMTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNEPDHTS SKMRLLFDLNAEVRTGYEIGKKMTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNGPDHTS ************************************	180 180 180 180
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	AHNLTEKQVGEDFKALHKVLEKYPTLNKGSLVGPDVGWMGVSYVKGLADGAGDLVTAFTL AHNLTEKQVGEDFKALHKVLEKYPTLNKGSPVGPDVGWMGVSYVKGLADGAGDLVTAFTL AHNLTEKQVGEDFKALHKVLEKYPTLNKGSLVGPDVGWMGVSXVKGLADEAGDHVTAFTL AHNLTEKQVGEDFKALHKVLEKYPTLNKGSLVGPDVGWMGVSYVKGLADEAGDHVTAFTL ************************************	240 240 240 240
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	HQYYFDGNTSDVSTYLDATYFKKLQQLFDKVKDVLKNSQHKDKPLWLGETSSGYNSGTKD HQYYFDGNTSDVSTYLDASYFKKLQQLFDKVKDVLKNSPHKDKPLWLGETSSGCNSGTKD HQYYFDGNTSDVSIYLDATYFKKLQQLFDKVKDVLKDSPHKDEPLWLGETSSGYNSGTED HQYYFDGNTSDVSIYLDATYFKKLQQLFDKVKDVLKDSPHKDKPLWLGETSSGYNSGTED ************************************	300 300 300 300
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYNGYYGLLDKNTLEPNPDYWLMHVHNSLV VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYNGYYGLLDKNTLEPNPDYWLMHVHNSLV VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYNGYYGLLDKNTLEPNPDYWLMHVHNSLV VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYSGYYGPLDKNTLEPNPDYWLMHVHNSLV	360 360
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	GNTVFKVDVSDPTNKARVYAQCTKTNSKHTQSRYYKGSLTIFALNVGDEDVTLKIDQYGG GNTVFKVDVGDPTNKTRVYAQCTKTNSKHTQGKYYKGSLTIFALNVGDEEVTLKIDQYGG GNTVFKVDVSDPTNKARVYAQCTKTNSKHTQSRYYKGSLTIFALNVGDGDVTLKIGQYSG GNTVFKVDVSDPTNKARVYAQCTKTNSKHTQSRYYKGSLTIFALNVGDEDVTLKIGQYSG ********* : **************************	420 420 420
SEQIDNO1. SEQIDNO3. SEQIDNO5.	KKIYSYILTPEGGQLTSQKVLLNGKELKLVSDQLPELNANESKTSFTLSPKTFGFFVVSD KKIYSYILTPEGGQLTSQKVLLNGKELNLVSDQLPELNADESKTSFTLSPKTFGFFVVSD KKIYSYILTPEGGQLTSQKVLLNGKELNLVSDQLPELNADESKTSFTLSPKTFGFFVVSD KKIYSYILTPEGGQLTSQKVLLNGKELNLVSDQLPQLNADESKTSFTLSPKTFGFFVVSD	480 480 480
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	ANVEACKK 488 ANVEACKK 488 ANVEACKK 488 ANVEACKK 488 ANVEACKK 488	-

CLUSTAL W (1.82) multiple sequence alignment

SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	KEIAVTIDDKNVIASVSESFHGVAFDASLFSPKGLWSFVDITSPKLFKLLEGLSPGYFRV 60 -KEIAVTIDDKNVIASVSESFHGVAFDASLFSPKGPWSFVNITSPKLFKLLEGLSPGYFRV 60 -KEIAVTIDDKNVIASASGSFLGVAFDASLFSPKGLWSFVDITSPKLFKLLEGLSPGYFRV 60
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	GGTFANWLFFDLDENNKWKDYWAFKDKTPETATITRRWLFRKQNNLKKETEDDLVKLTKG 120 GGTFANWLFFDLDENNKWKDYWAFKDKTPETATITRRWLFRKQNNLKKETFDDLVKLTKG 120 GGTFANWLFFDLDENNKWKDYWAFKDKTPETATITRRWLFRKQNNLKKETFDNLVKLTKG 120 GGTFANRLFFDLDENNKWKDYWAFKDKTPETATITRRWLFRKQNNLKKETFDNLVKLTKG 120 ***** *******************************
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	SKMRLLFDLNAEVRTGYEIGKKMTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNEPDHTS 180 SKMRLLFDLNAEVRTGYEIGKKTTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNEPDHTS 180 SKMRLLFDLNAEVRTGYEIGKKMTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNEPDHTS 180 SKMRLLFDLNAEVRTGYEIGKKMTSTWDSSEAEKLFKYCVSKGYGDNIDWELGNGPDHTS 180 ************************************
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	AHNLTEKQVGEDFKALHKVLEKYPTLNKGSLVGPDVGWMGVSYVKGLADGAGDLVTAFTL 240 AHNLTEKQVGEDFKALHKVLEKYPTLNKGSPVGPDVGWMGVSYVKGLADGAGDLVTAFTL 240 AHNLTEKQVGEDFKALHKVLEKYPTLNKGSLVGPDVGWMGVSXVKGLADEAGDHVTAFTL 240 AHNLTEKQVGEDFKALHKVLEKYPTLNKGSLVGPDVGWMGVSYVKGLADEAGDHVTAFTL 240 ************************************
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	HQYYFDGNTSDVSTYLDATYFKKLQQLFDKVKDVLKNSQHKDKPLWLGETSSGYNSGTKD 300 HQYYFDGNTSDVSTYLDASYFKKLQQLFDKVKDVLKNSPHKDKPLWLGETSSGCNSGTKD 300 HQYYFDGNTSDVSIYLDATYFKKLQQLFDKVKDVLKDSPHKDEPLWLGETSSGYNSGTED 300 HQYYFDGNTSDVSIYLDATYFKKLQQLFDKVKDVLKDSPHKDKPLWLGETSSGYNSGTED 300 ***********************************
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYNGYYGLLDKNTLEPNPDYWLMHVHNSLV 360 VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYNGYYGLLDKNTLEPNPDYWLMHVHNSLV 360 VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYNGYYGLLDKNTLEPNPDYWLMHVHNSLV 360 VSDRYVSGFLTLDKLGLSAANNVKVVIRQTIYSGYYGPLDKNTLEPNPDYWLMHVHNSLV 360 ************************************
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	GNTVFKVDVSDPTNKARVYAQCTKTNSKHTQSRYYKGSLTIFALNVGDEDVTLKIDQYGG 420 GNTVFKVDVGDPTNKTRVYAQCTKTNSKHTQGKYYKGSLTIFALNVGDEEVTLKIDQYGG 420 GNTVFKVDVSDPTNKARVYAQCTKTNSKHTQSRYYKGSLTIFALNVGDGDVTLKIGQYSG 420 GNTVFKVDVSDPTNKARVYAQCTKTNSKHTQSRYYKGSLTIFALNVGDEDVTLKIGQYSG 420 ********* :***************************
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	KKIYSYILTPEGGQLTSQKVLLNGKELKLVSDQLPELNANESKTSFTLSPKTFGFFVVSD 480 KKIYSYILTPEGGQLTSQKVLLNGKELNLVSDQLPELNADESKTSFTLSPKTFGFFVVSD 480 KKIYSYILTPEGGQLTSQKVLLNGKELNLVSDQLPELNADESKTSFTLSPKTFGFFVVSD 480 KKIYSYILTPEGGQLTSQKVLLNGKELNLVSDQLPQLNADESKTSFTLSPKTFGFFVVSD 480 ************************************
SEQIDNO1. SEQIDNO7. SEQIDNO3. SEQIDNO5.	ANVEACKK 488 ANVEACKK 488 ANVEACKK 488 ANVEACKK 488 ******